

# Mortality of a Cohort of Workers in the Styrene-Butadiene Polymer Manufacturing Industry (1943-1982)

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A cohort of 12,110 male workers employed 1 or more years in eight styrene-butadiene polymer (SBR) manufacturing plants in the United States and Canada has been followed for mortality over a 40-year period, 1943 to 1982. The all-cause mortality of these workers was low [standardized mortality ratio (SMR) = 0.81] compared to that of the general population. However, some specific sites of cancers had SMRs that exceeded 1.00. These sites were then examined by major work divisions. The sites of interest included leukemia and non-Hodgkin's lymphoma in whites. The SMRs for cancers of the digestive tract were higher than expected, especially esophageal cancer in whites and stomach cancer in blacks. The SMR for arteriosclerotic heart disease in black workers was significantly higher than would be expected based on general population rates.

Employees were assigned to a work area based on job longest held. The SMRs for specific diseases differed by work area. Production workers showed increased SMRs for hematologic neoplasms and maintenance workers, for digestive cancers. A significant excess SMR for arteriosclerotic heart disease occurred only in black maintenance workers, although excess mortality from this disease occurred in blacks regardless of where they worked the longest. A significant excess SMR for rheumatic heart disease was associated with work in the combined, all-other work areas. For many causes of death, there were significant deficits in the SMRs.

## Introduction

The synthetic rubber industry began in the United States in 1942 under the control of the federally sponsored Rubber Reserve Company, a part of the Reconstruction Finance Corporation (1). The plants were operated initially by privately owned companies and later were sold by the government to private industry. In the early years, all plants manufactured styrene-butadiene rubber (SBR), although, at some time in their histories, most companies manufactured other synthetic rubbers and related materials. Initially, 15 plants were built in the U.S. and 1 in Canada—all similar in design. One additional plant with the same design was built in the 1950s and also manufactured SBR. The common features of plant design and product manufacture in these companies provided a unique opportunity for an epidemiologic study. At the start of the study in 1977, 10 of these plants were still in operation. The cohort for study

was developed using the records from 8 of the 10 plants. The National Institute of Occupational Safety and Health (NIOSH) included the remaining 2 plants in their epidemiologic studies (1). Two of these facilities included in the original cohort ended operations in 1978 and 1984, but these plants and their workers still have been followed in the current study.

The basic method of producing synthetic rubber involves an emulsion polymerization process in which aqueous monomers of 1,3-butadiene and styrene are combined in the presence of a soap solution and an initiator system such as *p*-methane hydroperoxide and sodium formaldehyde sulfoxylate in combination with a mercaptan. When the desired level of polymerization is reached, an inhibiting agent, such as sodium dimethyldithiocarbamate, is added to the mixture to end the reaction. The unreacted monomer of 1,3-butadiene is recovered through distillation, and the styrene monomer is stripped by steam for reuse. Antioxidants, such as diphenylamine, are added to extend the life of the product. The latex is coagulated using salt and sulfuric acid. The coagulate is then washed and dried, and the crumb is prepared for shipment.

Several other chemicals may be added to SBR, such as carbon black, which is added to latex prepared for tire production, and extender oils, which change the proper-

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ties of the rubber. Other curing agents, accelerators, retarders, antioxidants, and antiozonants may be added depending on the final intended use of the latex.

All plants can be divided into work areas based on the manufacturing process. The geographic locations of work areas within the plant differ depending on specific plant layouts. The tank farm receives shipments of the monomers of styrene and 1,3-butadiene and pumps them to the various parts of the plant where needed. Located close to each other are the reactor area, where the polymerization takes place in glass-lined steel reactors, and the recovery area, where the unreacted monomers styrene and 1,3-butadiene are removed from the latex. The final steps in production occur in the coagulation area where chemicals that are prepared or stored in pigment preparation are added to the latex. Finishing includes all final steps such as extrusion, drying, baling, and any other steps that result in a product ready for shipping.

The plants require a large maintenance work force especially in trades, such as plumbing, pipefitting, carpentry, and welding. All plants have auxiliary utilities for operation such as power, refrigeration, and water treatment units. In addition they have laboratories involved in quality control for production and usually others for research and development. Most plants produce rubbers and plastics other than styrene-butadiene rubber. Some plants make these other products in a separate area with a specific crew; other plants use the same line where SBR is produced. Pilot plants at the facilities test new processes or changes in current methods. Some plants currently manufacture or have manufactured raw materials used in the production of SBR.

## Background of Study

In 1976, two leukemia cases were reported among workers in two Texas SBR plants. The National Institute for Occupational Safety and Health (NIOSH) conducted a cohort study of the workers in these plants and reported an excess risk of leukemia in one of the two plants (1). The risk of leukemia in the population hired in 1943 through 1945 was 2.12 times higher than the risk for U.S. males, but the difference was significant only when a one-sided test was used. Several cases occurred in workers with short employment and latency and those who were first hired during World War II when the industry was starting.

Previous studies of the rubber industry had focused primarily on tire manufacture. McMichael and collaborators (2) however, had noted that lymphatic and hematopoietic cancers occurred more frequently among workers in the synthetic rubber manufacturing area of the plant. In a subsequent publication, these investigators associated the leukemia risk with solvent exposure only and did not mention a relationship to the SBR department (3).

In 1977, a cohort study of rubber workers from eight

operating SBR polymer manufacturing plants was initiated. The results of this study indicated that the overall mortality of these workers was low compared to that of the general population, and no significant differences in site-specific cancer risks occurred (4,5). At the time the original study was initiated, styrene was a suspected carcinogenic chemical in this industry.

In recent years, toxicologic evidence focused attention on the potential carcinogenic effect of 1,3-butadiene rather than styrene (6). A cohort study of the mortality of workers at a 1,3-butadiene manufacturing plant demonstrated a significant risk of lymphosarcomas that was 2.35 times higher than that of the general population of the U.S. The risk appeared in workers who had routine exposures to 1,3-butadiene (7). They represented those employed in processing, laboratory, receiving, storage, and transport.

Since there was some toxicologic data but limited epidemiologic data regarding potential carcinogenic effects of 1,3-butadiene, it seemed worthwhile to follow-up the original cohort of SBR production workers to identify any possible risks from this chemical. From the time of the original study, the average age of the workers would have increased with a resultant increase in the number of deaths. Since the original cohort was already large, the study would have substantial power to demonstrate any risks that might exist. The present study, therefore, evaluates the total mortality of the original cohort of rubber workers for 40 years, examines the risks of specific cancers and other diseases compared to the general population, and evaluates the variation in the risks by major plant divisions.

## Description of Study

The original study cohort consisted of workers in the eight U.S. and Canadian styrene-butadiene polymer manufacturing plants that were in operation in 1976. All but one of the plants had started production in 1942 and 1943 when the synthetic rubber industry began in the U.S. The original cohort was established by abstracting the personnel records of each plant and by using computerized records of current workers in one plant. Information on name, birthdate, social security number for U.S. workers, and dates of hiring and termination was abstracted for each worker. The data for all employees from all plants were combined into a common, computerized data base.

A job listing was formed that included the job titles and work areas abstracted from the individual personnel files. Tasks required for the performance of each job were defined from employment requisitions and job descriptions that were provided by the plant. The jobs were grouped into broad work areas or departments that were usually listed as part of the job in the work history of each employee. The work area groupings are the same as those that were used to determine the mortality experience of workers in the original study (5). At the time of this study, the jobs had not been reviewed

by company industrial hygienists to identify exposures by job and to assure that the groupings within and across plants were correct.

A review of the personal records indicated that not all plants had complete data on all employees from the beginning of plant operations. All available records were abstracted and the start of the complete cohort for follow-up was determined by identifying the earliest year from which all possible lengths of employment occurred. This was the point from which record retention was considered complete. The start of plant production, which is the beginning of the cohort, and the start of follow-up are shown for each plant in Table 1. As can be seen from these data, limited mortality information will be gained from the two plants in which the follow-up starts in 1964 and 1970 with all workers who were employed at that time and all newly hired workers. These cohorts are heavily weighted with young and new employees. However, all plants have been included in the analysis.

The total population is defined as all individuals who were hired at the plants at some time between the start of production to December 1976 for complete cohorts, or who were working at the time of complete record-keeping, or were hired after that time to the end of 1976 for plants where all records were not retained. The total number of workers included in the population was 28,937 (Table 2). The population size has changed slightly from that of the original study because of editing, which removed duplicates and corrected records. Additional information from company files resulted in vital record searches on 2604 more workers than in the first study. However, most of the added information related to short-term employees who were eliminated from the study population by definition.

**Table 1. Cohort or production and follow-up start dates by plant.**

Plant	Cohort start	Follow-up start
1	October 1957	1964
2	September 1943	1958
3	September 1943	1943
4	July 1943	1970
5	January 1943	1953
6	March 1943	1943
7	October 1943	1943
8	July 1943	1943

**Table 2. Total workers and total cohort after exclusions (by order of exclusions).**

Cohort definitions	Number
Total subjects	28,937
Exclusion variables	
Females	4,238
Worked less than 1 year	9,022
Left before complete record keeping	1,073
Hired after 1976	711
Birth year missing or wrong	411
Total exclusions	15,515
Total cohort	13,422

The study cohort for follow-up was defined as only males who had either worked 1 year and who had been hired after the start of production in the plant or had worked at anytime after record keeping was complete until the end of cohort accrual on December 31, 1976. As can be seen from Table 2, 58% of all exclusions worked less than 1 year. Most of the remaining exclusions represent female workers and those who left employment before the start of follow-up in each plant. The 13,422 employees included in the follow-up cohort were traced for vital status to the end of 1982. A total of 11,155 workers or 82.5% of the population had worked in the four plants that had complete follow-up of all employees from the start of production. The fifth plant had included a complete cohort of all workers employed from early in production in 1953 and all new employees from that time forward. Thus, the population represents most workers who started employment in these eight plants at the beginning of the industry.

### Follow-up of Population

The vital status of each worker has been determined for the U.S. plants through the death notification system of the Social Security Administration and the National Death Index, as well as through follow-up by local plant beneficiary records and motor vehicle administration records. The vital status of individuals who were not working in 1982 were traced through these sources. For any individual who was identified as deceased, a death certificate was sought from the local health department. Death certificates were obtained for 97.2% of the study cohort deaths. The vital status of workers in the Canadian plant could only be determined through company records because of the high cost of a death search through Statistics Canada. However, the Canadian company has a pension and insurance plan that identifies all deaths among employees who worked 10 years or more or reached age 45 during employment. This cohort definition is similar to that of early studies of the rubber industry (8). For the analyses presented in this report, the Canadian population has been restricted to workers defined in this way. For known deaths in Canada, death certificates were obtained. All deaths were coded to the Eighth Revision of the International Classification of Causes of Death by a senior nosologist. A physician resolved all questions about disease diagnoses. Thus, the coding of deaths is similar for all plants.

In the previous study of this cohort, direct follow-up of a sample of the population identified previously unrecognized deaths through contact with respondents. If the fact of death was confirmed through retrieval of a certificate, the death was included. Otherwise, the subjects were counted as alive since respondents often could not provide any details about the death.

The mortality analysis included the follow-up cohort of all U.S. plants and, for the Canadian plant, those cohort members who worked 10 years or more or reached age 45 while still employed. This population is designated as the restricted cohort. As seen in Table 3, the vital status

**Table 3. Vital status of restricted cohort study population followed to December 31, 1982.**

Vital status	Number	Population
Living, employed in plant	2,784	23.0
Living, not in plant	6,472	53.4
Deceased	2,441	20.2
Status unknown	416	3.4
Total	12,113	100.0

was known for 96.6% of these workers. About 20% of the cohort are currently deceased. The group living "employed in plant" in this table designates those workers who were identified as still working in some plants.

## Job Categories

The job dictionary created by the investigators categorized each job by five characteristics: plant division, subdivision, work area, job title, and rank whenever applicable. If the worker's history designated a job only, a division was assigned to the job or based on the usual division in which that job appeared. (Recent discussions with process engineers from the industry have indicated that a few of these work areas or division assignments may have resulted in misclassification, but it was impractical to recode the work histories at that time since the study was complete.) The work history of each employee was reviewed and the first job, the last job, and the longest job held were coded for each worker. One or more of these jobs might not be coded for an individual worker if either all or part of the employment history was missing. If a worker had no history, no job was coded. If 50% or more of the work history was missing for the period of employment, no listing of longest job could be determined. In some cases, no listing was included for the first or last job. For one plant, no work histories were available for all workers employed at the time of filming of personnel files in 1976, because the active employees were identified from a computerized roster in that plant.

## Analysis

The data were analyzed using cumulative person-years of follow-up for each individual by age and calendar-time in the study cohort. These person-years were then multiplied by the appropriate U.S. rates for white and black males to determine the expected number of deaths. This represents the number of deaths that would have occurred had the workers died at the same rate as the general population. The modified life-table program available from Monson (9) was used for the analysis but not for significance testing.

The program allows for several modifications that eliminated any early worker experience in the industry before the start of follow-up. Since workers were included only if they had worked for 1 year, the first year of work experience was omitted from the sum of follow-up years. Workers' person-years of experience were only included from the time plant records were complete, thus avoiding the error of including the early

experience of workers who continued employment until start of cohort follow-up. Since the study of the population in the Canadian plant was restricted to employees working 10 or more years or reaching age 45 years while employed, the person-years at risk prior to 10 years of employment or age 45 were omitted to meet these eligibility criteria.

The Canadian population has been compared to population rates for both Canada and Ontario. The results were similar using either comparison population, so only the analyses with Ontario rates are discussed.

The deaths among workers are compared to the reference populations using an indirect adjustment for age, race, and calendar-year of death. The results are expressed as standardized mortality ratios or SMRs that are calculated as the observed deaths among workers divided by the deaths which would have occurred, had they died at the same rate as the reference population with a similar age, race, and time distribution to that of the workers. Thus, the ratio will be 1.00 if the workers and the reference population have the same risk of dying. The usual healthy-worker effect seen in working populations is apparent for most causes of death in this cohort as well.

Statistically significant excess standardized mortality ratios (SMR) are indicated for those causes which include more than one death. Significance was based on a probability of 0.05 or less (two-tailed) using the Poisson distribution.

## Results

The known racial distribution of the population was 75% white, 10% black, 15% unknown, and less than 1% other. However, the racial distribution differs by plant, depending on geographic location. Company personnel made extensive efforts to identify missing information on race from all record sources. However, 15% of the population still had unknown race and therefore were considered white in the analysis. Two plants had missing data on race for 40 to 50% of the workers. However, in only one of these plants is the omission a problem, since the population is predominantly white in all other plants with missing data. Because of the difficulty in determining an appropriate algorithm to assign race to workers without data, any worker with missing race information was assumed to be white. Death certificate data indicating race were used to update the records. Any error that this assumption has caused in the race-adjusted rates must be small since the population is predominantly white.

A total of 2,441 deaths are included in the analysis and 15.6% of them occurred in blacks. This indicates a slightly higher representation of blacks among the deaths than the 9.5% found in the total population. This difference may be due to an artificial inflation of the proportion of whites in the living white population through the inclusion of workers who have no race information or simply a higher mortality in blacks.

The cohort for analysis that restricted the Canadian population to persons with 10 or more years employment includes 12,100 workers who contributed 251,431 person-years of follow-up (Table 4). Three individuals had attained 100 or more years of age and are rejected by the analysis program. No attempt was made to alter information to force their inclusion in the analysis. The current analysis cohort is smaller than in the original study (13,608) because of data corrections and the restriction on the Canadian study population (5). However, death ascertainment is probably equally complete in U.S. and Canadian plants when applying this constraint.

The distribution of the population by race and entry into follow-up in the 10-year calendar periods and the median age of workers at entry for each period are shown in Table 5. A large number of workers entered follow-up at the start of the industry in plants with complete cohorts. In the next two 10-year decades, entries represent not only new employees but older workers who start follow-up at late ages because they belong to the plants with incomplete records or to the Canadian plant with the 10-year restriction on employment. Even in the first calendar period with complete

cohorts for follow-up, the age at entry is older than one might expect in a newly developed industry. In fact, for the black workers in the two calendar periods 1943 through 1949 and 1970 onward, which would represent complete cohorts of all workers who started in those periods, the age at start was 9 years older for those in the early period, compared to the late time frame.

The standardized mortality ratios by 5-year calendar time periods, as presented in Table 6, are very low (SMR = 0.37; 95% CI: 0.25–0.53) in the early years of follow-up probably because of the hiring of new healthy workers and rise to 0.87 in 1980 and 1982 when the closed population that remained after 1976 is continuing in follow-up. The mortality ratios increase more in the black than the white workers by calendar period. In fact, the SMR for black workers reaches a high of 1.34 (CI: 1.01–1.75) in the final 3-year period of follow-up. However, all ratios in all time periods among white workers indicate that their mortality is low compared to that of the general population.

The standardized mortality ratios for specific causes of death for white and black workers and for the total population adjusted for age, race, and calendar time are presented in the following tables. All results are based on the restricted follow-up cohort in Canada. For the major categories of death (Table 7) the mortality ratios are generally lower than expected, based on population rates. For most causes, white workers and the total population have death rates that are significantly lower than that of the U.S., as demonstrated by the fact that the upper confidence interval is less than 1.00. The only significantly high ratios in this table are those associated with deaths from arteriosclerotic heart disease (ASHD) and the related umbrella category, circulatory system diseases, found in black workers. The ratio for ASHD is 48% higher than would be expected based on population

Table 4. Characteristics of restricted cohort population for analysis.

Population	White	Black	Total
Total cohort	10,915 <sup>a</sup>	1,195	12,110
Total person-years of follow-up	226,474.80	24,956.20	251,431
Average survival from start of follow-up	20.75	20.88	20.8
Average age of entry into follow-up	34.08	32.82	34.0
Observed deaths	2,061	380	2,441

<sup>a</sup>Includes 1,767 with unknown race and 62 with other race.

Table 5. Distribution of population by year and median age of entry into follow-up.

Calendar period	White	Median age	Blacks	Median age	Total
1943–1949	2,210	33.9	418	36.3	2,628
1950–1959	3,134	34.9	246	32.7	3,380
1960–1969	3,190	30.6	268	28.8	3,458
1970+	2,381	31.3	263	27.3	2,644
Total	10,915	32.7	1,195	31.3	12,110

Table 6. All-cause standardized mortality ratios by race and calendar year of death (reference population: U.S. males).

Calendar year	White			Black			Total	
	Deaths	SMR <sup>a</sup>	95% CI <sup>a</sup>	Deaths	SMR	95% CI	SMR	95% CI
1943–49	22	0.40	0.25–0.61	7	0.30	0.12–0.61	0.37	0.25–0.53
1950–54	71	0.79	0.62–1.00	17	0.54	0.31–0.86	0.73	0.58–0.89
1955–59	135	0.80	0.69–0.97	33	0.84	0.58–1.18	0.80	0.69–0.94
1960–64	203	0.76	0.65–0.86	40	0.77	0.55–1.05	0.76	0.67–0.87
1965–69	313	0.78	0.69–0.87	64	0.96	0.74–1.23	0.81	0.73–0.90
1970–74	445	0.83	0.76–0.92	76	1.01	0.80–1.26	0.85	0.78–0.92
1975–79	509	0.80	0.73–0.87	89	1.22	0.98–1.50	0.84	0.78–0.91
1980–82	363	0.82	0.73–0.91	54	1.34	1.01–1.75	0.87	0.79–0.95
Total	2061	0.79	0.76–0.83	380	0.95	0.85–1.05	0.81	0.78–0.85

<sup>a</sup>SMR, standardized mortality ratio; 95% CI, 95% confidence interval based on Poisson distribution.

**Table 7. Standardized mortality ratios for major causes of death adjusted for age, calendar time, and race (reference population: U.S. males).**

Cause of death <sup>a</sup>	White (10,915)			Black (1,195)			Total (12,110)	
	Observed	SMR <sup>b</sup>	95% CI <sup>b</sup>	Observed	SMR	95% CI	SMR	95% CI
All causes	2,061	0.79	0.76–0.83	380	0.95	0.85–1.05	0.81	0.78–0.85
All cancers	454	0.85	0.77–0.92	64	0.92	0.71–1.18	0.85	0.78–0.93
All infections	17	0.54	0.32–0.87	9	0.62	0.28–1.17	0.57	0.37–0.83
Nervous system disease	22	0.96	0.60–1.45	3	0.78	0.16–2.28	0.93	0.60–1.38
Circulatory system disease	1,063	0.80	0.75–0.85	214	1.18	1.03–1.35	0.85	0.81–0.89
ASHD	772	0.84	0.78–0.90	125	1.48	1.23–1.76	0.89	0.84–0.95
Vascular CNS	141	0.85	0.72–1.01	47	1.18	0.87–1.57	0.92	0.79–1.06
RHD	20	0.86	0.53–1.33	1	0.36	—	0.81	0.50–1.24
Respiratory disease	106	0.68	0.56–0.82	18	0.79	0.47–1.24	0.69	0.58–0.83
Digestive disease	66	0.51	0.40–0.65	14	0.72	0.39–1.21	0.54	0.43–0.67
Genito-urinary disease	23	0.68	0.43–1.02	7	0.58	0.23–1.19	0.65	0.44–0.93
All external causes	174	0.69	0.59–0.80	39	0.77	0.55–1.05	0.70	0.61–0.80

<sup>a</sup>ASHD, arteriosclerotic heart disease; CNS, central nervous system; RHD, rheumatic heart disease.

<sup>b</sup>SMR, standardized mortality ratio; 95% CI, 95% confidence interval based on Poisson distribution.

rates (SMR = 1.48; 95% CI: 1.23–1.76).

The SMRs for most cancer sites that included five or more deaths (Table 8), are below 1.00, indicating that the risks of these cancers in the workers are less than those of the general population. For some cancers such as those of the kidney, digestive, and lymphohematopoietic system the risks approach those of the reference population. This is somewhat unusual for workers with low overall risks. Since the current update was prompted by toxicologic data relating 1,3-butadiene exposure to development of certain tumors, further analysis has focused on cancers of related biologic systems in humans. These systems include the gastrointestinal, hematopoietic, and lymphatic systems. Extensive evaluation of these sites was conducted, even though the SMRs related to these cancers often were only slightly above 1.00.

The specific sites in the digestive system (Table 8) that seem to contribute a higher risk than others are esophageal cancers in whites (SMR = 1.34; 95% CI: 0.78–2.14), stomach cancers in all workers (SMR = 1.05; 95% CI: 0.73–1.46), cancer of the large intestine in whites (SMR = 0.93; 95% CI: 0.68–1.25), and liver cancers in black workers (SMR = 1.44; 95% CI: 0.30–4.19). The sites of cancer that are high in the hematopoietic system are Hodgkin's disease in whites (SMR = 1.31; 95% CI: 0.56–2.58), leukemia in blacks (SMR = 2.18; 95% CI: 0.59–5.60), and other lymphatic cancers in all workers (SMR = 1.11; 95% CI: 0.64–1.77). None of the ratios is significantly higher than 1.00. The number of deaths in some groups is very small. Nevertheless, it was felt on the basis of these data that further analysis by work area was warranted in order to identify specific patterns of risk. These, in turn, could suggest

**Table 8. Standardized mortality ratios for selected cancers adjusted for age, calendar time, and race (reference population: U.S. males).**

Cancers	White (10,915)			Black (1,195)			Total (12,160)	
	Observed	SMR <sup>a</sup>	95% CI <sup>a</sup>	Observed	SMR	95% CI	SMR	95% CI
Oral cavity	5	0.30	0.10–0.69	0	0	—	0.26	0.08–0.60
Digestive	137	0.94	0.79–1.11	21	0.92	0.57–1.41	0.93	0.79–1.09
Esophagus	17	1.34	0.78–2.14	0	0	—	1.00	0.58–1.61
Stomach	25	0.95	0.62–1.41	9	1.45	0.66–2.76	1.05	0.73–1.46
Large intestine	45	0.93	0.68–1.25	3	0.67	0.14–1.96	0.91	0.67–1.21
Rectum	11	0.70	0.35–1.24	1	0.62	—	0.69	0.36–1.20
Liver	8	0.75	0.32–1.48	3	1.44	0.30–4.19	0.86	0.43–1.54
Pancreas	24	0.83	0.53–1.23	3	0.80	0.17–2.35	0.83	0.54–1.20
Respiratory	157	0.83	0.70–0.98	20	0.93	0.57–1.43	0.84	0.72–0.98
Prostate	28	0.82	0.54–1.18	9	1.18	0.54–2.24	0.88	0.62–1.22
Bladder	11	0.72	0.36–1.28	1	0.67	—	0.71	0.37–1.24
Kidney	15	1.11	0.62–2.05	0	0	—	1.03	0.58–1.69
Brain	14	0.85	0.47–1.43	0	0	—	0.81	0.44–1.36
All lymphopietic	48	0.92	0.68–1.23	7	1.46	0.59–3.01	0.97	0.73–1.26
Lymphosarcoma	6	0.56	0.21–1.22	1	1.32	—	0.61	0.25–1.26
Hodgkin's	8	1.31	0.56–2.58	0	0	—	1.20	0.52–2.37
Leukemia	18	0.86	0.51–1.36	4	2.18	0.59–5.60	0.96	0.60–1.46
Other lymphatic	15	1.10	0.62–1.81	2	1.16	0.14–4.20	1.11	0.64–1.77

<sup>a</sup>SMR, standardized mortality ratio; 95% CI, 95% confidence interval based on Poisson distribution.

that different exposures might be associated with the risks.

The total population ratios were standardized for region using Ontario rates as a comparison for the Canadian population and the U.S. rates for other areas. These ratios do not differ from those presented previously. For example, the all-cause SMR was 0.83 after adjustment for region compared to 0.81 in the previous analysis. The only differences of note were a decrease in the SMR for stomach cancer, from 1.05 unadjusted to 0.91 adjusted, and an increase in the all lymphopoietic category from 0.97 to 1.06.

## Work Areas

The population was divided into four major work areas on the basis of the job held the longest. Three plant divisions, production, utilities, and maintenance, and the combination of all other work sites constituted the four groups for analysis (Table 9). These divisions are similar to those in the original study (5). No attempt has

been made in this analysis to combine jobs or work areas by presumed exposures, although one might assume that production will include more exposures than other work sites, with the possible exception of the laboratories. The purpose of the analysis was to divide the population into major work activities in order to determine whether there are any different patterns of risk. The production grouping includes workers involved in any processes that produce the rubber and who may, therefore, have had some exposure to the basic chemicals that form the raw product. Maintenance includes workers exposed to materials related to their trades and incidental exposures to the agents used in the industrial processes. Utilities represent support facilities whose workers may have exposures to specific agents. Finally, the other-job category includes warehouse, laboratory, and administration work sites. This diverse group had workers who probably had exposures in laboratories and other workers such as administrative personnel who received no exposure.

Since a classification of longest job required complete job history records, 2391 workers (19.7%) who had gaps in their work history were omitted from these analyses. The plant that provided a computer tape of current workers in 1976 had limited job information on the active population, and this group represents 75% of all persons omitted from the work area analysis. The loss of person-years from the low risk group of recent, healthy, active workers may have artificially inflated the SMRs reported by work areas.

An examination of the specific causes of death in production workers adjusted for age, race, and time (Table 10) shows low mortality for all causes (SMR = 0.88; 95% CI: 0.81–0.95) and cancers (SMR = 0.92; 95% CI: 0.76–1.09). However, deaths from cancers of the hematologic system occurred at higher rates than expected (SMR = 1.46; 95% CI: 0.88–2.27). The ratio for black workers is 5 times higher than the mortality expected in U.S. black males and is significant (SMR = 5.07; 95% CI: 1.87–11.07). The ratio for the whites is near unity (SMR = 1.10; 95% CI: 0.58–1.87). Among the subcategories, there is no excess risk of lymphosarcoma. The ratio for Hodgkin's disease is greater than one in white workers, but it is based on only two deaths. The SMR for leukemia is 0.84 for white males (SMR = 0.84; 95% CI: 0.22–2.15), but the SMR indicates a significant excess risk in black workers, which is 6.6 times higher than expected in comparable groups (SMR = 6.56; 95% CI: 1.35–19.06). The total race-adjusted ratio is above one (SMR = 1.34; 95% CI: 0.53–2.76) but not significant. For the categories of other lymphomas that includes cases of non-Hodgkin's lymphomas as well as multiple myeloma, the ratios are high for both races and significantly high in the total population, with a 2.6-fold excess risk in the rubber workers compared in U.S. males (SMR = 2.60; 95% CI: 1.99–4.94). These cases represent four non-Hodgkin's lymphomas and five multiple myelomas according to the death certificates. On the other hand, the risk of death from digestive system

Table 9. Work areas and jobs included in analysis by work history.

Work area	Job	
Production	Tank farm	
	Pigment preparation or solution make-up	
	Reactor—control meters, inspect reactors, blowdown latex	
	Recovery—stripping styrene and butadiene	
	Finishing	
	Latex blending—addition of brine	
	Coagulation—addition of sulfuric acid	
	Washing and drying	
Warehouse and shipping	Baling and packaging	
	Reclaiming	
Utilities	Boiler house operator	Pump house operator
	Water tower operator	Refrigeration operator
Maintenance	Boilermaker	Sheetmetal
	Carpenter	Water gun operator or water truck driver
	Electrician	Welder
	Instrument repair	General (engineers)
	Insulator	Millwright
	Machinist	Mason
	Mechanic	Blacksmith
	Oiler	Ironworkers
	Painter	
	Pipefitter	
Laboratory and quality control		
Research and development		
Administration		
Other	Drivers	Janitors
	Environmental controls	Kitchen
	Firemen	Medical
	Guards	Safety

**Table 10. Standardized mortality ratios of production workers for selected causes of death adjusted for age, calendar-time, and race (reference population: U.S. males).**

Cause <sup>a</sup>	White (2,753)			Black (371)			Total (3,124)	
	Observed	SMR <sup>b</sup>	95% CI <sup>b</sup>	Observed	SMR	95% CI	SMR	95% CI
All causes	502	0.87	0.79–0.94	92	0.93	0.75–1.14	0.88	0.81–0.95
Circulatory System								
disease	254	0.89	0.78–1.01	49	1.16	0.86–1.54	0.93	0.82–1.04
ASHD	182	0.91	0.78–1.05	29	1.47	0.99–2.11	0.96	0.83–1.10
Vascular CNS	37	1.08	0.76–1.48	9	0.99	0.45–1.88	1.06	0.77–1.41
RHD	5	0.93	0.30–2.16	1	0.69	—	0.99	0.36–2.14
All cancers	105	0.88	0.72–1.07	19	1.15	0.69–1.79	0.92	0.76–1.09
Respiratory	43	1.03	0.74–1.39	6	1.14	0.42–2.48	1.04	0.77–1.38
Larynx	1	0.57	—	0	0	—	0.49	—
Lung	41	1.03	0.74–1.40	6	1.23	0.45–2.67	1.06	0.78–1.40
Digestive	25	0.79	0.51–1.16	3	0.56	0.11–1.64	0.75	0.50–1.09
Esophagus	3	1.08	0.22–3.15	0	0	—	0.79	0.16–2.30
Stomach	3	0.53	0.11–1.56	1	0.70	—	0.57	0.15–1.45
Large intestine	10	0.95	0.46–1.75	1	0.96	—	0.95	0.48–1.70
Rectum	2	0.58	0.07–2.11	0	0	—	0.53	0.06–1.90
Liver	0	0	—	1	1.98	—	0.36	—
Pancreas	5	0.79	0.26–1.84	0	0	—	0.69	0.22–1.62
Kidney	5	1.66	0.54–3.88	0	0	—	1.53	0.50–3.57
All lymphopoeitic	13	1.10	0.58–1.87	6	5.07	1.87–11.07	1.46	0.88–2.27
Lymphosarcoma	0	0	—	1	5.32	—	0.38	—
Hodgkin's	2	1.31	0.16–4.75	0	0	—	1.20	0.15–4.35
Leukemia	4	0.84	0.22–2.15	3	6.56	1.35–19.06	1.34	0.53–2.76
Other								
Lymphatic	7	2.30	0.92–4.73	2	4.82	0.59–17.62	2.60	1.19–4.94

<sup>a</sup>ASHD, arteriosclerotic heart disease; CNS, central nervous system; RHD, rheumatic heart disease.

<sup>b</sup>SMR, standardized mortality ratio; 95% CI, 95% confidence interval based on Poisson distribution.

cancers is very low in this work group (SMR = 0.75; 95% CI: 0.50–1.09) with the exception of cancer of the large intestine, which approaches unity (SMR = 0.95; 95% CI: 0.48–1.70). The only other cancer ratios which deserve comment are lung (SMR = 1.06; 95% CI: 0.78–1.40) and kidney (SMR = 1.53; 95% CI: 0.50–3.57).

Mortality from diseases of the circulatory system in production workers is higher than usual for a working population. Usually occupational populations of healthy workers have low mortality from this group of diseases. The excess is particularly notable for ASHD in black males where the excess is 47% above that expected (SMR = 1.47; 95% CI: 0.99–2.11).

For workers who had held their longest job in maintenance (Table 11), the all-cause SMR is 0.90 (95% CI: 0.85–1.06) and the cancer SMR is 0.95 (95% CI: 0.83–1.10). There are no excesses of hematologic neoplasms with the exception of a nonsignificant excess of Hodgkin's disease, based on only three deaths (SMR = 1.51; 95% CI: 0.31–4.41). Unlike production workers, individuals engaged in maintenance work have SMRs for cancers of the digestive system that exceed one, although they are not significant (SMR = 1.06; 95% CI: 0.81–1.35). The risk is higher in white workers (SMR = 1.11; 95% CI: 0.84–1.45) than in black workers (SMR = 0.78; 95% CI: 0.34–1.53). For white workers, mortality from stomach cancer is 66% higher (SMR = 1.66; 95% CI: 0.93–2.75), intestinal cancers 11% higher (SMR = 1.11; 95% CI: 0.66–1.75), and esophageal cancers 44% higher than expected in the general population (SMR = 1.44; 95% CI: 0.53–3.14). Three testicular cancer deaths versus 0.95 expected (SMR = 3.16) occurred in the total

population, and they were all in white maintenance workers.

Both the risk of arteriosclerotic heart disease (SMR = 1.76; 95% CI: 1.36–2.33) as well as the risk of the combined category of circulatory disease (SMR = 1.38; 95% CI: 1.14–1.66) are significantly high in blacks who worked in maintenance jobs, but white workers have a SMR of only 0.91 for ASHD (95% CI: 0.81–1.03). The excess mortality from circulatory system disease probably accounts for the excess of all-cause mortality in black maintenance workers (SMR = 1.05; 95% CI: 0.91–1.21). The excess risk of ASHD in black workers appears in production area employees as well, even though the excess is not significantly high in that group. Vascular lesions of the central nervous system (CNS) occur at a slightly higher than expected rate in blacks in this population (SMR = 1.30; 95% CI: 0.83–1.94). Further investigation of the excesses of ASHD must determine the reasons for these excesses.

The 457 workers who staff the power and refrigeration plants and work in general utilities have an overall mortality ratio of 0.93 (95% CI: 0.77–1.11) (Table 12). The numbers in any disease subcategory are too small to reach firm conclusions about any risks. In general, the SMRs are higher among those specific causes that were also high for the other work groups, that is, digestive and respiratory system cancers and hematologic neoplasms.

Workers with complete job histories who were not included in the previous three work areas are combined into a single mixed group as shown in Table 13. The mortality ratios for this group of workers for all causes



**Table 11. Standardized mortality ratios of maintenance workers for selected causes of death adjusted for age, calendar-time, and race (reference population: U.S. males).**

Cause <sup>a</sup>	White (2,828)			Black (443)			Total (3,271)	
	Observed	SMR <sup>b</sup>	95% CI <sup>b</sup>	Observed	SMR	95% CI	SMR	95% CI
All causes	751	0.87	0.81–0.94	186	1.05	0.91–1.21	0.90	0.85–1.06
Circulatory system disease	381	0.84	0.76–0.93	114	1.38	1.14–1.66	0.92	0.84–1.01
ASHD	287	0.91	0.81–1.03	67	1.76	1.36–2.33	1.01	0.90–1.12
Vascular CNS	43	0.72	0.52–0.97	24	1.30	0.83–1.94	0.86	0.66–1.09
RHD	3	0.41	0.08–1.18	0	0	—	0.35	0.07–1.01
All cancers	174	0.99	0.84–1.14	24	0.78	0.50–1.16	0.95	0.83–1.10
Respiratory	60	0.99	0.75–1.27	8	0.86	0.37–1.69	0.97	0.75–1.23
Larynx	0	0	—	0	0	—	0	—
Lung	59	1.03	0.78–1.33	8	0.92	0.40–1.82	1.01	0.79–1.29
Digestive	55	1.11	0.84–1.45	8	0.78	0.34–1.53	1.06	0.81–1.35
Esophagus	6	1.44	0.53–3.14	0	0	—	1.00	0.37–2.17
Stomach	15	1.66	0.93–2.75	3	1.04	0.21–3.04	1.51	0.90–2.39
Large intestine	18	1.11	0.66–1.75	1	0.50	—	1.04	0.63–1.62
Rectum	5	0.92	0.30–2.15	1	1.37	—	0.97	0.36–2.12
Liver	1	0.28	—	0	0	—	0.22	—
Pancreas	8	0.83	0.36–1.64	1	0.60	—	0.80	0.36–1.51
Kidney	5	1.15	0.37–2.69	0	0	—	1.04	0.34–2.43
All lymphopoietic	14	0.85	0.46–1.42	0	0	—	0.75	0.41–1.26
Lymphosarcoma	2	0.59	0.07–2.12	0	0	—	0.53	0.06–1.93
Hodgkin's	3	1.70	0.35–4.95	0	0	—	1.51	0.31–4.41
Leukemia	6	0.88	0.32–1.92	0	0	—	0.79	0.29–1.72
Other lymphatic	2	0.46	0.06–1.65	0	0	—	0.39	0.05–1.41

<sup>a</sup>ASHD, arteriosclerotic heart disease; CNS, central nervous system; RHD, rheumatic heart disease.

<sup>b</sup>SMR, standardized mortality ratio; 95% CI, 95% confidence interval based on Poisson distribution.

**Table 12. Standardized mortality ratios of utility workers for selected causes of death adjusted for age, calendar-time and race (reference population: U.S. males).**

Causes	Observed	SMR <sup>a</sup>	95% CI <sup>a</sup>
All causes	126	0.93	0.77–1.11
All cancers	30	1.13	0.77–1.62
Digestive cancers	8	1.05	0.45–2.06
Large intestine	4	1.61	0.44–4.13
Respiratory cancers	13	1.49	0.79–2.55
Larynx	2	5.13	0.62–8.52
Lung cancers	10	1.22	0.58–2.24
Lymphopoietic cancers	5	2.03	0.66–4.74
Leukemia	2	1.92	0.23–6.95
Other lymphatic	2	3.13	0.62–6.95

<sup>a</sup>SMR, standardized mortality ratio; 95% CI, 95% confidence interval based on Poisson distribution.

and cancer are low, 0.85 (95% CI: 0.79–0.92) and 0.84 (95% CI: 0.70–1.01), respectively. Only the mortality from rheumatic heart disease in white workers is significantly high with an SMR of 2.09 (95% CI: 1.08–3.65). Mortality from chronic nephritis is also high (SMR = 1.89; 95% CI: 0.61–4.40) but not significant. These sites would not be expected to be associated with industry exposures unless there is misdiagnosis since they are usually associated with an infectious etiology.

Many other ratios for this group exceed one but they are not significant, and there is no apparent pattern as noted for the other two major work areas. The SMRs that exceed one are those that were high in work areas previously reviewed, such as digestive tract cancers and stomach cancers in blacks and larynx cancers, leukemia, and Hodgkin's disease in white. The sites that have mortality ratios above expected specifically for this area are: liver cancers, with seven cases in both races (SMR

= 2.24; 95% CI: 0.90–4.61), pancreas cancers, with ten cases also in all workers (SMR = 1.26; 95% CI: 0.61–2.32), and brain cancer in whites only (SMR = 1.25; 95% CI: 0.41–2.92). This work group needs to be redefined in order to distinguish subgroups that may have had different exposures.

An attempt to identify any association between hematologic neoplasms and the years worked in the rubber industry for the total cohort of workers is shown in Table 14. In general, these analyses show no increase in risk by duration worked or latency. The greatest number of person-years fall in the diagonal with a comparable number of years worked and years from first employment. A large proportion of current employees contribute person-years to that group, but not deaths. At most, half of this population could only contribute person-years in categories with 10 or more years of employment. Therefore, a clear trend is difficult to identify. However, the SMR is 1.34 (95% CI: 0.83–2.05) for long-term workers who have been followed for 10 years or more from first employment (latent period) and who worked 10 to 19 years.

## Discussion

The total population of workers in the synthetic rubber industry show no significant excess in mortality from any specific cause of death adjusted for age, race, and time. As reported in the original study, there is a significant excess of arteriosclerotic heart disease among black employees. That group demonstrates a 45% increase in mortality over that expected based on U.S. black male rates. The significant 18% increase in all circulatory

**Table 13. Standardized mortality ratios of workers in "other" category for selected causes of death adjusted for age, calendar-time and race (reference population: U.S. males).**

Cause <sup>a</sup>	White (2,630)			Black (237)			Total (2,867)	
	Observed	SMR <sup>b</sup>	95% CI <sup>b</sup>	Observed	SMR	95% CI	SMR	95% CI
All causes	545	0.85	0.78-0.92	79	0.90	0.71- 1.12	0.85	0.79-0.92
Circulatory system disease	301	0.92	0.82-1.03	40	1.01	0.72- 1.38	0.93	0.83-1.03
ASHD	208	0.92	0.80-1.05	21	1.12	0.69- 1.71	0.93	0.82-1.06
Vascular CNS	47	1.13	0.83-1.51	12	1.38	0.71- 2.41	1.18	0.90-1.52
RHD	12	2.09	1.08-3.65	0	0	—	1.90	0.98-3.31
All cancers	105	0.80	0.65-0.96	19	1.23	0.75- 1.95	0.84	0.70-1.01
Respiratory	32	0.70	0.48-0.99	6	1.25	0.46- 2.73	0.75	0.53-1.04
Larynx	3	1.54	0.32-4.50	0	0	—	1.35	0.28-3.93
Lung	29	0.67	0.45-0.96	6	1.35	0.49- 2.93	0.73	0.51-1.02
Digestive	35	0.97	0.67-1.34	8	1.60	0.69- 3.15	1.04	0.75-1.40
Esophagus	2	0.64	0.08-2.32	0	0	—	0.50	0.06-1.78
Stomach	5	0.75	0.24-1.75	4	2.97	0.81- 7.59	1.12	0.51-2.13
Large intestines	10	0.85	0.41-1.55	1	1.00	—	0.86	0.43-1.53
Rectum	2	0.51	0.06-1.82	0	0	—	0.46	0.06-1.68
Liver	5	1.88	0.61-4.37	2	4.39	0.53-15.71	2.24	0.90-4.61
Pancreas	9	1.27	0.58-2.41	1	1.20	—	1.26	0.61-2.32
Kidney	1	0.30	—	0	0	—	0.28	—
All lymphopoietic	11	0.86	0.43-1.54	1	0.94	—	0.87	0.45-1.52
Lymphosarcoma	1	0.38	—	0	0	—	0.36	—
Hodgkin's	2	1.30	0.16-4.72	0	0	—	1.22	0.15-4.41
Leukemia	6	1.16	0.43-2.52	1	2.46	—	1.25	0.50-2.58
Other lymphatic	2	0.61	0.07-2.20	0	0	—	0.54	0.07-1.96

<sup>a</sup>ASHD, arteriosclerotic heart disease; CNS, central nervous system; RHD, rheumatic heart disease.<sup>b</sup>SMR, standardized mortality ratio; 95% CI, 95% confidence interval based on Poisson distribution.**Table 14. Standardized mortality ratios age, race, and time adjusted by duration of employment and by years since first employment: lymphatic and hematopoietic cancers.**

Years worked	Time from first employment (latency), years									
	< 10		10 - 19		20 - 29		30 - 39		Total	
	Observed	SMR	Observed	SMR	Observed	SMR	Observed	SMR	Observed	SMR
< 10	3	0.46	2	0.42	4	0.73	7	1.65	16	0.76
10-19			14	1.31	3	0.84	4	2.74	21	1.34
20-29					14	1.28	0	0.00	14	0.96
30-39							4	0.72	4	0.72
Total	3	0.46	16	1.03	21	1.05	15	1.02	55	0.97

disease reflects this increase in arteriosclerotic heart disease, as well as a small nonsignificant increase of 18% in deaths from vascular lesions of the central nervous system. There is no known industrial exposure that explains these excesses. How much this difference has resulted from the bias of having racial information on all deaths and not on all living workers is unknown. Since any worker with unknown race is assumed to be white, the mortality ratios for blacks are overestimated and whites are underestimated to the extent that race for unknown workers is erroneously classified. Therefore, the total SMRs are probably the most correct representation of risk.

Canadian mortality rates provided by Statistics Canada for both Canada and Ontario were used for geographic adjustment. In general, the results did not differ when this correction was added. The grouping of major disease rates differed between Canada and the U.S. mortality data. This variation and possible discrepancies in some rates made it practical to use U.S. rates for all work area analysis.

Since ratios for the total population do not provide any discrimination as to exposures of the population for analysis, a first step in examining potential work place hazards is the division of the population into large work areas. In this study, individuals were assigned to four work areas, based on longest job held. Deaths from cancers of the hematopoietic and lymphopoietic system are higher than expected in production workers with significant excesses for leukemias in black workers and other lymphomas in all workers. Although these cancers occur in excess for workers in utilities and the other miscellaneous work group, the ratios are not as high. For the large number of workers in maintenance, there is no excess risk of hematologic cancers but a higher than expected mortality for various cancer sites in the digestive tract. Production workers do not have this excess. Although the mortality for these digestive system cancers may not be significantly different from that of the reference population, the completely different cancer sites that show an excess mortality for maintenance versus production workers suggest that variation in

exposures in the two groups might be playing a role. Although it is possible that, especially for stomach cancer, ethnicity or socioeconomic factors may be playing a role and that different ethnic groups may hold different jobs in the industry, this explanation seems less likely than the attribution of the differences to exposures related to their work. These differences in cancers by work areas are also interesting because of their consistency among a limited number of sites. All hematologic neoplasms except lymphosarcoma have mortality ratios above 1.0 for production workers. The specific digestive system cancers that occur in excess in maintenance workers are esophagus, stomach, and large intestine. Workers employed in administration and the other combined work sites including laboratories have different causes of death that occur in excess than either in production or maintenance workers. Chronic rheumatic heart disease and even chronic nephritis have high mortality ratios in these workers. One might postulate that these excesses may reflect the bias of selecting workers who were not eligible to serve in the military in the early years of the industry and were employed in sedentary, nonphysically demanding jobs in administration. This observation needs to be examined further. However, the group also had a high risk of liver and pancreatic cancers that could not be explained by the same selection bias. The risk for laboratory personnel included in this group should be examined separately since they may be the source of these cancer risks. Confirmation of the information on disease outcome and work history is essential.

Missing information on total work history has forced the exclusion of 2391 workers in these tables. Many of those omitted were active workers in 1976 and are more likely to be alive than dead at the end of the study. This would mean deceased workers and their person-years represent a higher proportion of the population that is included in the calculation of expected deaths for the work area analysis, compared to the total population mortality analysis. This omission of work histories in living workers results in an all-cause mortality ratio for the combined work areas of 0.88, which, although still below one, is higher than the ratio for the total study cohort (SMR = 0.81). This higher percentage of deceased workers could result in higher cause-specific ratios by work area than those seen in the total population. However, these results would not explain the differences in risks of specific causes of death by work areas since the missing work histories for active employees would have occurred for all work areas.

Since the risks of specific causes of death such as hematologic neoplasms seem to be slightly higher than that of the general population, and, since these causes seem to be associated with different work areas, this population needs further study. The exposures by job must be identified including those related to this specific industry, such as 1,3-butadiene and styrene, as well as those associated with trades, such as welders and pipe fitters. The differences in risks for production and main-

tenance workers may suggest that industrial exposures are related to the cancers found in the former group, and the exposures related to a trade may be related to the digestive system cancers. An assessment of estimated levels of exposure to 1,3-butadiene and styrene for each job is necessary and should be used in a case-control study.

## Summary

The mortality of workers in the styrene-1,3-butadiene polymer manufacturing industry is generally much lower than that of comparable populations. However, an excess risk of death from hematologic neoplasms, especially leukemia and other lymphomas, in production workers suggests that a further examination of exposures associated with work in this industry is warranted. The small excess of digestive system cancers among maintenance workers may represent risks associated with their specific trades or industrial exposures.

**NOTE ADDED TO PROOF:** In a follow-up nested case-control study in which the cases of lymphopoeitic cancers were compared to an internal population of workers who did not have cancer, we found that the leukemia cases were associated with exposure specifically to butadiene (odds ratio: 9.4; 95% confidence interval: 2.1–22.9), whereas there was not a significantly increased risk associated with exposure to styrene [Matanoski et al., ILSI Monograph: Assessment of Inhalation Hazards (1989)].

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